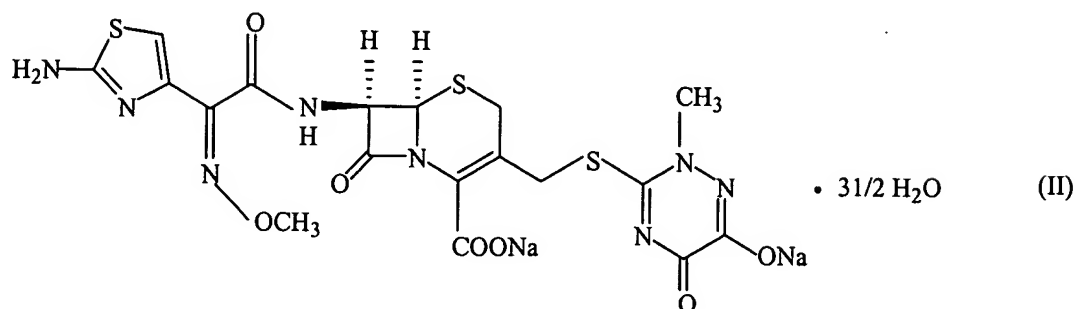


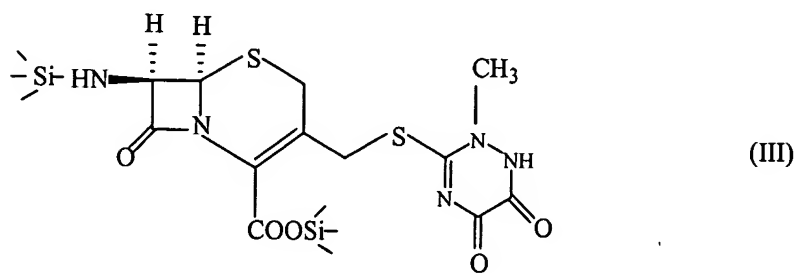
We claim:

1. In a process for preparation of ceftriaxone sodium of formula (II),

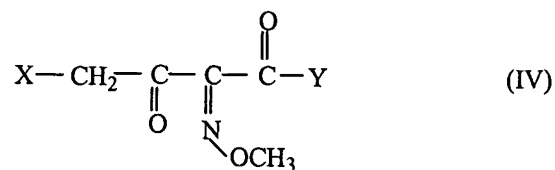


comprising the steps of

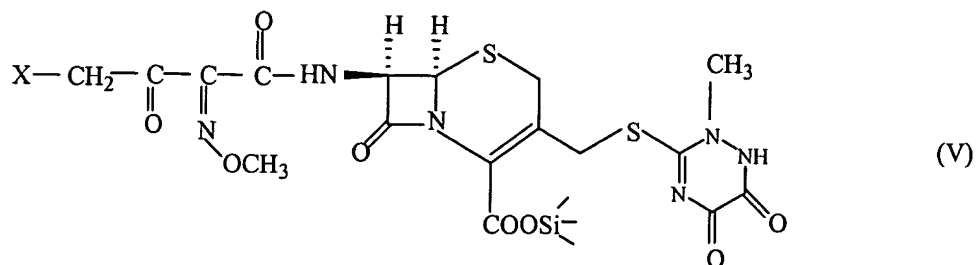
- i) reacting a silylated compound of formula (III),



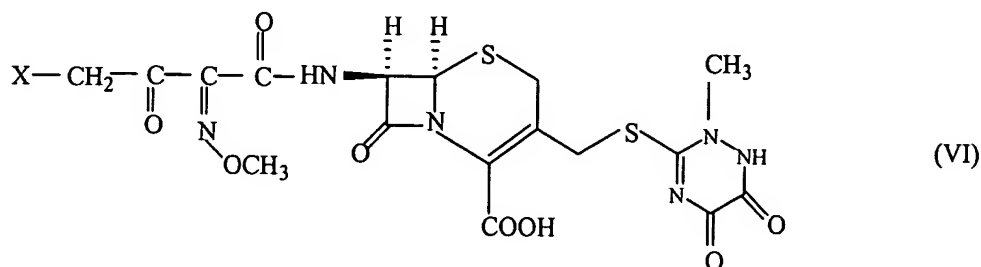
with a 4-halo-2-methoxyimino-3-oxo-butyric acid derivative of formula (IV),



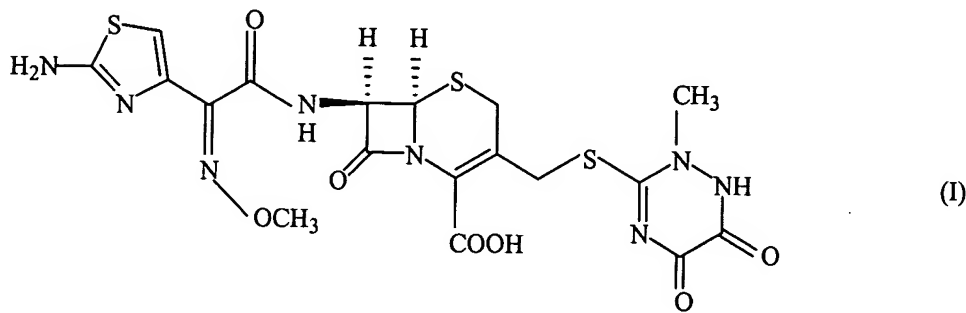
wherein X and Y represent a halogen atom to give a compound of formula (V),



- ii) desilylating the compound of formula (V), wherein X is as defined hereinabove to give the desilylated compound of formula (VI),

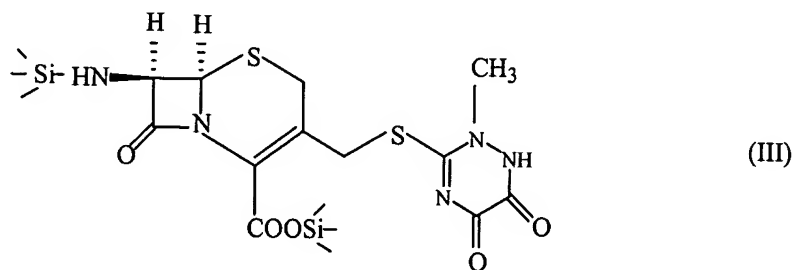


- iii) reacting the desilylated compound of formula (VI) with thiourea in a solvent system containing organic solvent and water, to obtain ceftriaxone of formula (I),

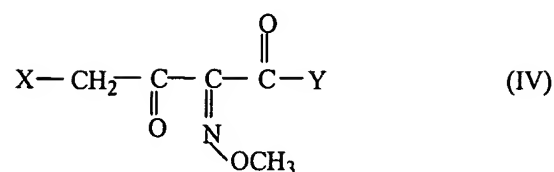


- iv) converting the compound of formula (I) to the sodium salt (II); **wherefore the improvement comprises**

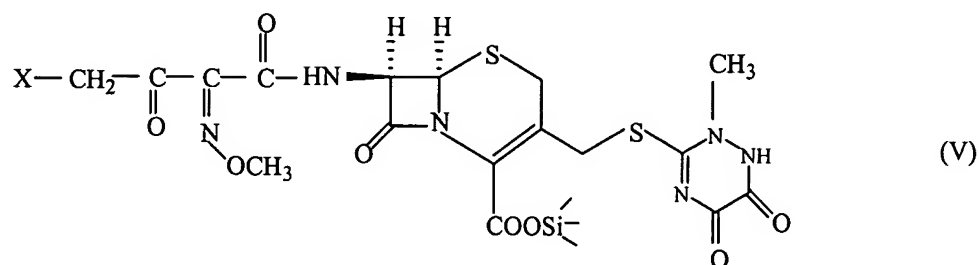
- i¹) reacting a silylated compound of formula (III),



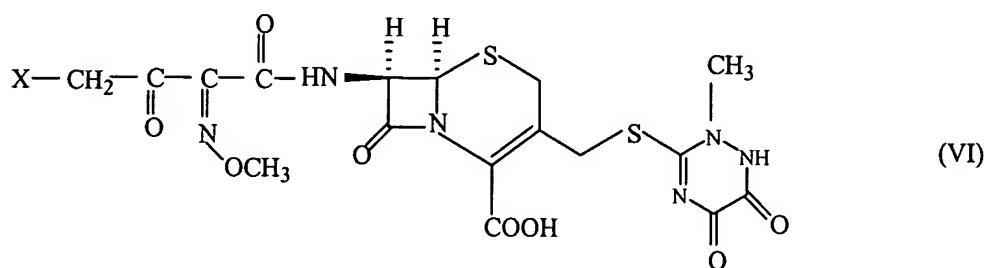
with a 4-halo-2-methoxyimino-3-oxo butyric acid derivative of formula (IV), having a purity of at least 95% and containing di- and poly-brominated compounds less than 0.50%,



wherein X and Y represent a halogen atom in the presence of an inert water-immiscible organic solvent or mixtures thereof and in the presence of an acid scavenging agent at a temperature of between -10° C to -0° C to give a compound of formula (V),



- ii¹) adding the solution of compound of formula (V) in the inert water-immiscible organic solvent or mixtures thereof to a 1:1 mixture of water and a water-immiscible organic solvent and separation of the organic phase to provide a solution of compound of formula (VI) in the inert water-immiscible organic solvent or mixtures thereof,



- iii¹) reacting the solution of compound of formula (VI) in the inert water-immiscible organic solvent or mixtures thereof with a solution of thiourea in water in the presence of an alkali metal containing inorganic base at a temperature of between 0° C to +10° C at a pH ranging between 5.0 to 5.5 and separation of the organic layer to provide a solution of the alkali metal salt of ceftriaxone of formula (II¹) in water, wherein M is an alkali metal,



iv¹⁾ mixing the solution of the alkali metal salt of ceftriaxone (II'), wherein M is as defined hereinafter in water with a water-immiscible organic solvent and a water-miscible solvent and treating the solution thus obtained with an acid to a pH of 3.6 to 4.0 and isolating the precipitated ceftriaxone of formula (I) by filtration,

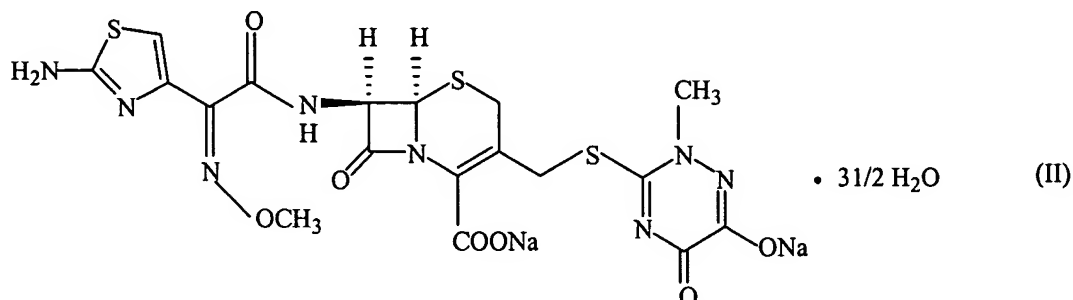


v¹) reacting a solution of ceftriaxone of formula (I) in water with an organic amine maintaining a pH of 5.4 ± 0.2 to produce a solution of the amine salt of ceftriaxone in water of formula (VII),



wherein Q represents the organic amine, and

- vi¹) reaction of the amine salt of ceftriaxone of formula (VII) in a mixture of water and a water-miscible organic solvent with a sodium metal carrier to give ceftriaxone sodium of formula (II), substantially free of impurities and having low color absorbance.



2. A process according to claim 1, in which in step i¹), the inert water-immiscible organic solvent is selected from chlorinated hydrocarbons, acetic acid (C₁₋₄) alkyl esters and ethers.
3. A process according to claim 1, in which in step i¹), wherein the acid scavenging agent is selected from ethylene oxide, propylene oxide, butylene oxide, acetamide, epichlorohydrin, calcium oxide, disodium hydrogen phosphate, calcium carbonate and quaternary ammonium phosphates.
4. A process according to any one of claims 1 and 2, wherein the preferred acid scavenging agent is acetamide.
5. A process according to any one of claims 1, 2 and 3, wherein the acid scavenging agent is employed in molar proportions of 1.0 to 3.0 moles per mole of compound of formula (III).
6. A process according to any one of claims 1, 2, 3 and 4, wherein the acid scavenging agent is employed in molar proportions of 1.0 to 1.5 moles per mole of compound of formula (III).

7. A process according to claim 1, in which in step ii¹), the water-miscible organic solvent is selected from tetrahydrofuran or acetonitrile.
8. A process according to claim 1, in which in step iii¹), thiourea is employed in molar proportions of 1.0 to 3.0 moles per mole of compound of formula (III), preferably in molar proportions of 1.0 to 1.5 moles per mole of compound of formula (III).
9. A process according to claim 1, in which in step iii¹), the alkali metal inorganic base is selected from sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate and lithium hydrogen carbonate.
10. A process according to any one of claims 1 and 9, wherein the alkali metal containing inorganic base is employed in molar proportions of 2.0 to 5.0 moles per mole of compound of formula (III), preferably in molar proportions of 2.0 to 3.0 moles per mole of compound of formula (III).
11. A process according to claim 1, in which in step iv¹), the water-immiscible organic solvent is selected from chlorinated hydrocarbons, acetic acid (C₁₋₄) alkyl esters and ethers.
12. A process according to claim 1, in which in step iv¹), the water-miscible organic solvent is selected from tetrahydrofuran, acetonitrile or a C₁₋₄ lower alcohol.
13. A process according to claim 1, in which in step v¹), the organic amine is selected from diethylamine, triethylamine, diisopropylamine, cyclohexylamine, pyridine, 2,4-dimethylamino pyridine and N-methyl morpholine.
14. A process according to claim 1, in which in step vi¹), the water-miscible organic solvent is selected from tetrahydrofuran, acetonitrile, a C₁₋₄ lower alcohol and a ketonic solvent.

15. A process according to claim 1, in which in step vi¹), the sodium metal carrier carrier is selected from sodium acetate, 2-ethyl sodium hexanoate and 2-ethyl sodium octanoate.
16. A process according to claim 1, wherein the ceftriaxone sodium of formula (II) has a color absorbance of 0.04 to 0.05 AU at 450 nm.
17. A process according to claim 1, wherein the level of total impurities in ceftriaxone sodium (II) obtained is the range of between 0.05 to 0.20%.